preparation of a compound of Formula I as claimed in claim 1…". Accordingly, claim 5 as amended now appears to be a process specifically adapted for the manufacture of the product of claim 1 as set forth in 37 CFR 1.475(b)(3). Additionally, claims 7 and 14-17 have been amended into proper method claim format in the U.S. The amendments do not introduce new matter within the meaning of 35 U.S.C. § 132. Accordingly, entry of the amendments is respectfully requested.

SUMMARY OF RESTRICTION REQUIREMENT

The Examiner has required restriction of claims 1-21 under PCT Rule 13.1 to a single general inventive concept encompassed by the claims as follows:

> This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. Due to the numerous variables in the claims, e.g. R1, R'1, R2, R3, R4, R5, R6, R7, R8, R9, etc., and their widely divergent meanings, a precise listing of inventive groups can not be made. The following groups are exemplary:
> **Group I** claim(s) 1-4, 6, and 11-13 drawn to products of the formula (I) wherein R1 is carboxyl, R2 is 1^{o}-3^{o} amino, R3 is -CH2-thioxanthyl, and R4 is carboxyl.
> **Group II** claim(s) 1-4, 6, and 11-13 drawn to products of the formula (I) wherein R1 is carboxyl, R2 is 1^{o}-3^{o} amino, R3 is -CH2-xanthyl, and R4 is carboxyl.
> **Group III** claim(s) 5 drawn to the process for preparing compounds of the formula (I) wherein R1 is carboxyl, R2 is 1^{o}-3^{o} amino, R3 is xanthyl, and R4 is carboxyl.
> **Group IV** claim(s) 7, and 14-17 drawn to methods of modulating metabotropic glutamate receptor functions with the compounds of the formula (I) wherein R1 is carboxyl, R2 is 1^{o}-3^{o} amino, R3 is thioxanthyl, and R4 is carboxyl.
> **Group V** claim(s) 8 drawn to compounds of the formula (II)

wherein R1 is carboxyl, R4 is carboxyl, and R5 is a (2-6C) alkanoyl group.

Group VI claim(s) 18-19 drawn to compounds of the formula (IIb) wherein R'1 is carboxyl, and R3 is H.

Group VII claim(s) 9, and 20-21 drawn to compounds of the formula (III) wherein R1 is carboxyl, R4 is carboxyl, R6 is a hydrogen or a (1-4C) alkyl group, and R7 is a hydrogen atom or a (1-4C) alkyl group.

Group VIII claim(s) 10 drawn to compounds of the formula (IV) wherein R1 is carboxyl, R4 is carboxyl, R8 is carboxyl, and R9 is hydrogen.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted. Again, this list is not exhausted as it would be impossible under the time constraints due to the sheer volume of subject matter instantly claimed. Therefore, applicant may choose to elect a single invention by identifying another specific embodiment not listed in the exemplary groups of the invention and the examiner will endeavor to group the same. If applicant wishes to elect subject matter other than that identified in the above groups, applicant may elect a species (e.g. 4-carboxycubane-1-methylglycine) and examiner will endeavor to group it.

The claims herein lack unity of invention under PCT Rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art. Claims 8, 9, 10, and 18 clearly have a different special technical feature than that of the cubane derivative of claim 1 (i.e. claim 9 has a hydantoin substituted cubane), and the compounds in inventions I-IV contain a cubane derivative, which does not define a contribution over the prior art. The substituents on the cubane derivative vary extensively and when taken as a whole result in vastly different compounds. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper. Additionally, the vastness of the claimed subject matter, and the complications in understanding the claimed subject matter imposes a burden on any examination of the claimed subject matter.

ELECTION

Applicants provisionally elect Group I, claims 1-4, 6, and 11-13, drawn to products of the formula (I) wherein R1 is carboxyl, R2 is 1^{o}-3^{o} amino, R3 is -CH2-thioxanthyl, and R4 is carboxyl, Group III, claim 5, drawn to the process for preparing compounds of the formula (I) wherein R1 is carboxyl, R2 is 1^{o}-3^{o} amino, R3 is -CH2-thioxanthyl, and R4 is carboxyl, and Group IV, claims 7 and 14-17, drawn to methods of modulating metabotropic glutamate receptor functions with the compounds of the formula (I) wherein R1 is carboxyl, R2 is 1^{o}-3^{o} amino, R3 is -CH2-thioxanthyl, and R4 is carboxyl, with traverse as each of these three Groups have unity of invention as they are drawn to a combination of a product, a process specially adapted for the manufacture of the said product, and a use of the said product as defined in 37 CFR 1.475(b)(3). In the event the Examiner requires election of a single group, applicants hereby provisionally elect Group I with traverse.

TRAVERSAL

Applicants respectfully traverse the Examiner's restriction requirement for the following reasons.

This application is the national stage of a PCT application; accordingly, it must be examined according to the restriction practice criteria of the PCT, under PCT Rule 13.1, which requires the grouping of inventions according to a single inventive concept. The PTO restriction procedure for such a national stage application

is set forth in 37 CFR 1.475. In particular, 37 CFR 1.475(b)(3) states that a national stage application will be considered to have unity of invention if the claims are drawn only to the combination of "A product, a process specially adapted for the manufacture of the said product, and a use of the said product". Accordingly, applicants have amended claim 5 to recite "A process for the preparation of a compound of Formula I as claimed in claim 1…"; accordingly claim 5 is now a process specifically adapted for the manufacture of the product of claim 1. Similarly, claim 7 already recites "A use of the compound according to claim 1…"; accordingly claims 7 and 14-17 relate to uses of the product of claim 1. Applicants respectfully assert that each of Groups I, III, and IV, then, have unity of invention and should all properly be examined in accordance with the rules for National Stage applications. In this regard, applicants note the elected invention is directed to where R3 is -CH2-thioxanthyl, not R3 is xanthyl or thioxanthyl as noted by the Examiner.

Further, the restriction requirement is improper because it omits "an appropriate explanation" as to the existence of a "serious burden" if a restriction were not required. (MPEP § 803). An examination of all the claims in this application would not pose a serious burden because a search of any one of invention Groups I through VIII would require searching the prior art areas

appropriate to the other invention Groups.

Lastly, applicants have paid a filing fee for an examination of all the claims in this application. If the Examiner refuses to examine the claims paid for when this application was filed, applicants must pay duplicative fees to file divisional applications for the non-elected or withdrawn groups of claims.

CONCLUSION

In view of the foregoing, applicants respectfully request the Examiner to reconsider and withdraw the restriction requirement and to examine claims 1-21 pending in this application.

If the Examiner has any questions or wishes to discuss this matter, the Examiner is welcomed to telephone the undersigned attorney.

Respectfully submitted,

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Date: 2 Dec, 2002

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PATENT
Attorney Docket No. 24406

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

CURRY et al. Examiner: R. Anderson

Serial No.: 09/673,473 Art Unit: 1626

Filed: November 29, 2000

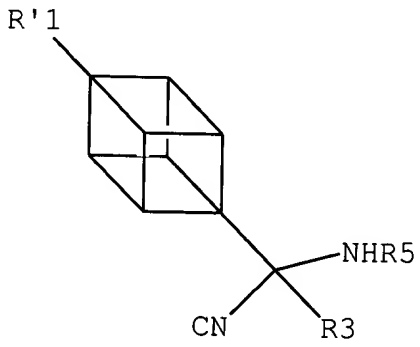
For: **CUBANE DERIVATIVES AS METABOTROPIC GLUTAMATE RECEPTOR AGONISTS OR ANTAGONISTS AND PROCESS FOR THEIR PREPARATION**

Appendix A

Please amend the following claim as indicated in the following marked up copy of the claims.

5. (Twice Amended) A process for the preparation of a compound of Formula I as claimed in claim 1, or a pharmaceutically acceptable metabolically-labile ester or amide thereof, or a pharmaceutically acceptable salt thereof, which comprises:

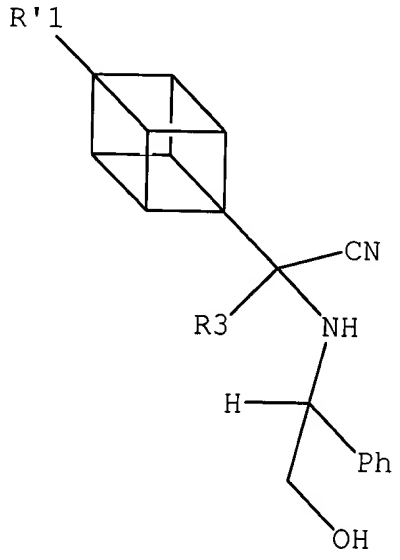
(a) hydrolyzing a compound of formula:



(II)

wherein: **R'1** is an acidic group selected from the group consisting of carboxyl, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol, -CH_2-carboxyl, -CH_2-phosphono, -CH_2-phosphino, -CH_2-sulfono, -CH_2-sulfino, -CH_2-borono, -CH_2-tetrazol, -CH_2-isoxazol and higher analogues thereof, or a protected form thereof, **R3** can be H, aliphatic, aromatic or heterocyclic and **R5** represents a hydrogen atom or an acyl group, and wherein preferred values for **R5** are hydrogen and (2-6C) alkanoyl groups, such as acetyl; or

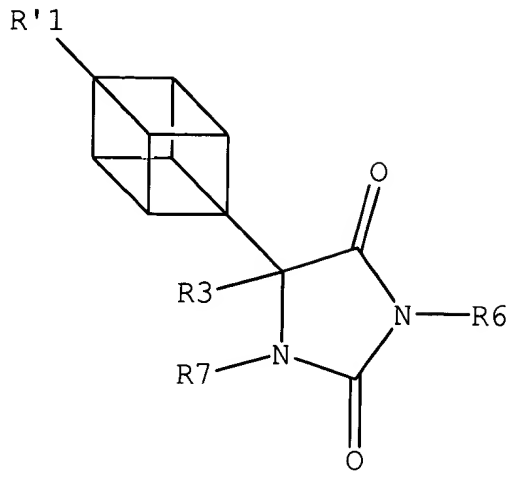
(b) deprotecting and hydrolyzing a compound of formula (IIb):



(IIb)

wherein: **R'1** and **R3** are as defined above; or

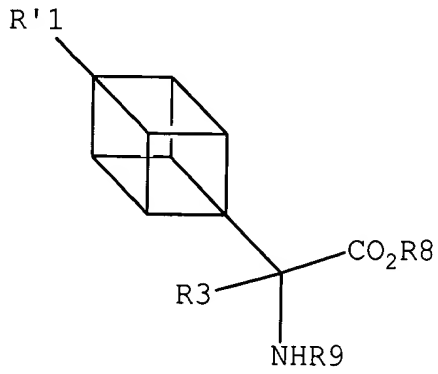
(c) hydrolyzing a compound of formula:



(III)

wherein: **R6** and **R7** each independently represent a hydrogen atom, a (2-6C) alkanoyl group, a (1-4C) alkyl group, a (3-4C) alkenyl group or a phenyl (1-4C) alkyl group in which the phenyl is unsubstituted or substituted by halogen, (1-4C) alkyl or (1-4C) alkoxy, or a salt thereof, **R'1** and **R3** are as defined above; or

(d) deprotecting a compound of formula:



(IV)

wherein: **R8** represents a hydrogen atom or a carboxyl protecting group, or a salt thereof, and **R9** represents a hydrogen atom or a nitrogen protecting group, **R'1** and **R3** are as defined above;

whereafter, if necessary and/or desired:

(i) resolving the compound of Formula I;

(ii) converting the compound of Formula I into a non-toxic metabolically-labile ester or amide thereof; and/or

(iii) converting the compound of Formula I or a non-toxic metabolically-labile ester or amide thereof into a pharmaceutically acceptable salt thereof.

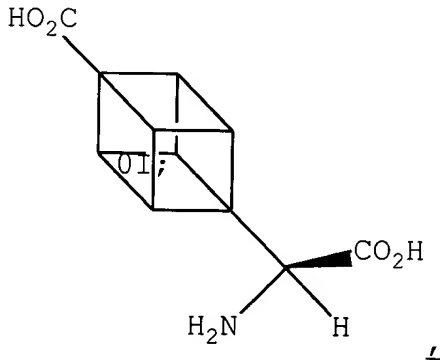
7. (Twice Amended) A method of modulating [use of the compound according to claim 1 to modulate] one or more metabotropic glutamate receptor functions in a warm blooded mammal, [wherein said use comprises] comprising administering an effective amount of a compound of formula (I) as claimed in claim 1 to a warm blooded mammal in need thereof.

14. (Once Amended) [A use of] A method of treating a neurological disease or disorder in a warm blooded mammal comprising administering an effective amount of the compound of formula (I) according to claim 1 to a warm blooded mammal in need thereof, wherein said [for the treatment of a] neurological disease or disorder is selected from the group consisting of [comprising:] cerebral deficits subsequent to cardiac bypass surgery and grafting, cerebral ischemia, stroke, cardiac arrest, spinal cord trauma, head trauma, perinatal hypoxia, and

hypoglycemic neuronal damage, Alzheimer's disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, ocular damage, retinopathy, cognitive disorders, idiopathic and drug-induced Parkinson's disease, muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, drug tolerance, withdrawal, and cessation (i.e. opiates, benzodiazepines, nicotine, cocaine, or ethanol), smoking cessation, anxiety and related disorders (e.g. panic attack), emesis, brain edema, chronic pain, sleep disorders, Tourette's syndrome, attention deficit disorder, and tardive dyskinesia[, wherein said use comprises administering an effective amount of a compound of formula (I)].

15. (Once Amended) [A use of] A method of treating a psychiatric disease or disorder in a warm blooded mammal comprising administering an effective amount of the compound of formula (I) according to claim 1 to a warm blooded mammal in need thereof, wherein said [for the treatment of a] psychiatric disease or disorder is selected from the group consisting of [comprising:] schizophrenia, anxiety and related disorders (e.g. panic attack), depression, bipolar disorders, psychosis, and obsessive compulsive disorders[, wherein said use comprises administering an effective amount of a compound of formula (I)].

16. (Once Amended) The [use] method according to claim 7 wherein said compound is selected from the group [of compounds comprising:] consisting of



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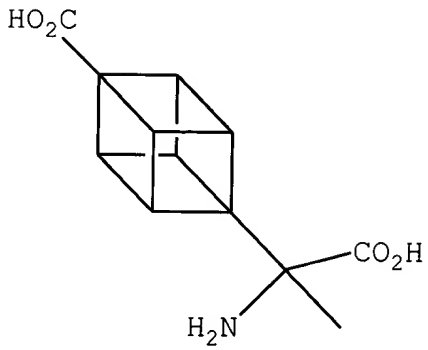

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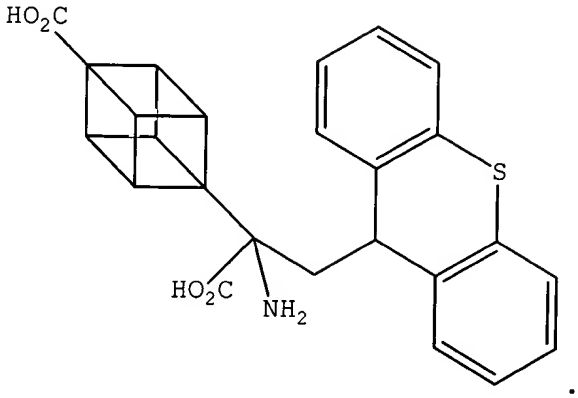

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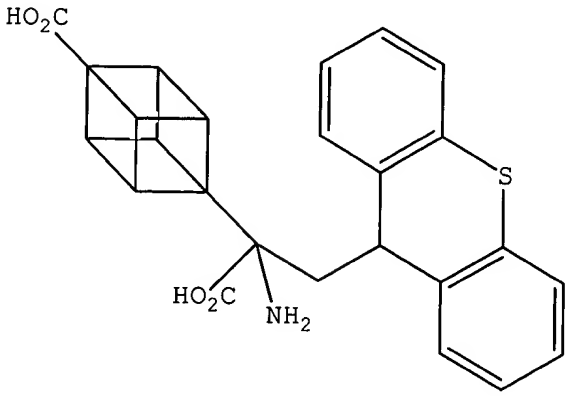
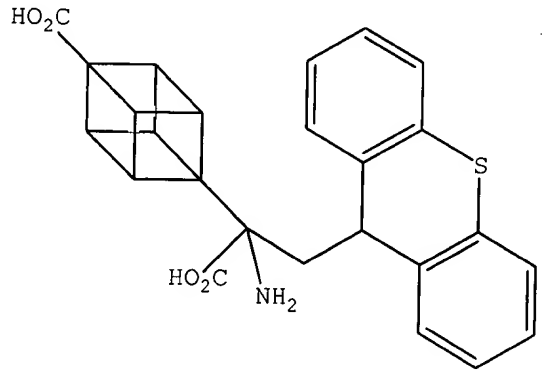
17. (Once Amended) A method of treating [use of the compound:



for the treatment of] cerebral ischemia, stroke and cardiac arrest in a warm blooded mammal comprising[, wherein said use comprises] administering an effective amount of the [said] compound



to a warm blooded mammal in need thereof.